reduction of the otic placode (Alvarez et al., Dev. 2003, Ladher et al., Genes and Dev. 2005, Wright and Mansour, Dev. 2003, Zelarayan et al., Dev. Bio. 2007). Our observation that the otic placode is expanded in Spry1$^{-/-}$;Spry2$^{-/-}$ double mutants is consistent with the possibility that Spry1 and Spry2 negatively regulate FGF-mediated induction of the otic placode. To test the possibility that Spry1 and Spry2 antagonize FGF signaling during otic placode induction, we have begun genetic interaction experiments between the Spry1, Spry2, and Fgf10 genes. Results from these genetic interaction experiments will be presented.

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Program/Abstract # 239
Canonical Notch signaling is neither necessary nor sufficient for prosensory induction in the mouse cochlea
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The mammalian organ of Corti consists of a highly organized pattern of hair cells and supporting cells that originate from a common population of prosensory progenitor cells. Several signaling pathways including BMP, FGF, SHH and Notch act in concert to achieve this fine grained pattern. The Notch signaling pathway has been well-characterized for its role in regulating differentiation in the organ of Corti through lateral inhibition. Notch signaling from the Jag1 ligand has also been proposed to have a second, earlier role in the specification of sensory progenitors in the inner ear. To examine the role of Notch signaling in these two processes, we conditionally inactivated RBPjk, the transcriptional effector of canonical Notch signaling, throughout the inner ear. We show that in the absence of RBPjk, the cochlear prosensory domain forms normally and hair cells and supporting cells differentiate. However, differentiating hair cells rapidly die in RBPjk mutants. The prosensory domain of the cochlea also differentiates normally in Jag1 conditional mutant mice. Finally, in contrast to the chick basilar papilla, activation of Notch in the mouse cochlea did not induce ectopic sensory patches. Our results indicate that canonical Notch signaling is neither necessary nor sufficient for prosensory specification in the mouse cochlea, suggesting that other signaling pathways are required for the specification of this highly derived sensory organ.

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Program/Abstract # 240
The role of Sox2 in the regulation of eye development
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The basic organization of eye tissues depends on interactions between cephalic ectoderm and optic vesicle. The transcription factor Sox2 plays pivotal roles in the development of both tissues. The Sox2 expression in the pre-placodal cephalic ectoderm is regulated by mainly enhancer N-4, while the same enhancer also participates in Sox2 regulation in the optic vesicle. We have investigated the function of Sox2 in the regulation of eye development, utilizing enhancer N-4 knockout mice. These mice showed the small eye phenotype in adulthood. We examined when this phenotype initiates, and found this traced back to the lens induction stage. The lens placode invagination in enhancer N-4 knockout embryo was delayed at E10.5. The molecular markers of cell differentiation, e.g. crystallins in lens, however, were normally expressed at E13.5, and the morphology of eye was not severely affected except that the sizes of both lens and retina remained smaller than wild type. This observation suggests that the delay of lens placode invagination is causative to the small eye development. An ongoing project is to see whether the ectodermal Sox2 downregulation is sufficient for causing small eyes.

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Program/Abstract # 241
Transcriptome profiling highlights multiple roles for Xrx1 during eye development
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Despite the crucial role played by Xrx1 in controlling eye field specification and maintenance of retinal stem cells multipotency, the genetic program regulated by this transcription factor remains to be largely deciphered. To identify the gene networks controlled by Xrx1, the transcriptome of control Xenopus embryos was compared to that of embryos overexpressing Xrx1 and embryos in which Xrx1 was knocked-down. This analysis, performed using Affymetrix microarrays, detected 44 transcripts displaying a coherent behaviour, i.e., showing increased levels of expression in the gain of function assay and decreased levels in loss of function experiments, or vice versa. In the vast majority of cases, these data have been confirmed by real time PCR and in situ hybridization. The identity of selected transcripts indicates multiple roles for Xrx1 in controlling different phases of retinal specification. These include the regulation of cell movements during eye field formation, the determination of eye field size, the maintenance of a pluripotent cell fate, and the repression of endomesodermal genes. In particular, the latter represents a novel, critical function for a retinal transcription factor, which appears to block, directly or indirectly, endomesodermal signals known to inhibit retinal fate.

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Program/Abstract # 242
pug function is essential for normal limb length
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The radiation of vertebrates to occupy aquatic, terrestrial, and aerial environments involved modifications to the size and shape of their limbs. Limb length is regulated by early signaling centers in the developing limb bud and later by proliferation and outgrowth of the skeletal precursor cells (chondrocytes). Defects in these later stages typically result in shorter, but normally patterned limbs (i.e. dwarfism). Despite recent advances in chondrocyte biology, our understanding of the factors that regulate bone length is incomplete. To expand our knowledge of these factors, we are currently working with a recessive mouse mutant. *pug* mutant limbs appear normal early, but by birth are only ~80% the length of wild-type limbs. Histological analyses revealed